

DTG, where the first amino acid of the first special set of amino acids is, the first special amino acid, D, and where the second set of amino acids is either DSG or DTG, where the last amino acid of the second set of special amino acids is the last special amino acid, G, where the first special amino acid is operably linked to amino acids that code for any number of amino acids from zero to 81 amino acid positions where in each position it may be any amino acid.

The amino acid polypeptide of claim 62, where the first special amino acid is operably linked to a peptide from about 30 to 77 amino acids positions where each amino acid position may be any amino acid. The amino acid polypeptide of claim 63, where the first special amino acid is operably linked to a peptide of 35, 47, 71, or 77 amino acids.

The amino acid polypeptide of claim 63, where the first special amino acid is operably linked to the same corresponding peptides from SEQ. ID. NO. 3 that are 35, 47, 71, or 77 peptides in length, beginning counting with the amino acids on the first special sequence, DTG, towards the N-terminal of SEQ. ID. NO. 3.

The amino acid polypeptide of claim 65, where the polypeptide comprises a sequence that is at least 95% identical to the same corresponding amino acids in SEQ. ID. NO. 4, that is, identical to that portion of the sequences in SEQ. ID. NO. 4, including all the sequences from both the first and or the second special nucleic acids, toward the N-terminal, through and including 71, 47, 35 amino acids before the first special amino acids. (Examples 10 and 11).

The amino acid polypeptide of claim 65, where the complete polypeptide comprises the peptide of 71 amino acids, where the first of the amino acid is T and the second is Q. The nucleic acid polynucleotide of claim 21, where the polynucleotide comprises a sequence that is at least 95% identical to the same corresponding amino acids in SEQ. ID. NO. 3, that is, identical to the sequences in SEQ. ID. NO. 3 including the sequences from both the first and or the second special nucleic acids, toward the N-Terminal, through and including 71 amino acids, see Example 10, beginning from the DTG site and including the nucleotides from that code for 71 amino acids).

The nucleic acid polynucleotide of claim 22, where the complete polynucleotide comprises identical to the same corresponding amino acids in SEQ. ID. NO. 3, that is, identical to the sequences in SEQ. ID. NO. 3 including the sequences from both the first and or the second special nucleic acids, toward the N-Terminal, through and including 71

amino acids, see Example 10, beginning from the DTG site and including the nucleotides from that code for 71 amino acids).

The nucleic acid polynucleotide of claim 18, where the first special nucleic acid is operably linked to nucleic acids that code for any number of from about 30 to 54 amino acids where each codon may code for any amino acid.

The nucleic acid polynucleotide of claim 20, where the first special nucleic acid is operably linked to 47 codons where the first those 35 or 47 amino acids is the amino acid E or G

The nucleic acid polynucleotide of claim 21, where the polynucleotide comprises a sequence that is at least 95% identical to the same corresponding amino acids in SEQ. ID. NO. 3, that is, identical to that portion of the sequences in SEQ. ID. NO. 3 including the sequences from both the first and or the second special nucleic acids, toward the N-Terminal, through and including 35 or 47 amino acids, see Example 11 for the 47 example, beginning from the DTG site and including the nucleotides from that code for the previous 35 or 47 amino acids before the DTG site). The nucleic acid polynucleotide of claim 22, where the polynucleotide comprises identical to the same corresponding amino acids in SEQ. ID. NO. 3, that is, identical to the sequences in SEQ. ID. NO. 3 including the sequences from both the first and or the second special nucleic acids, toward the N-Terminal, through and including 35 or 47 amino acids, see Example 11 for the 47 example, beginning from the DTG site and including the nucleotides from that code for the previous 35 or 47 amino acids before the DTG site).

An isolated nucleic acid molecule comprising a polynucleotide, said polynucleotide encoding a Hu-Asp polypeptide and having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a nucleotide sequence encoding a Hu-Asp polypeptide selected from the group consisting of Hu-Asp1, Hu-Asp2(a), and Hu-Asp2(b), wherein said Hu-Asp1, Hu-Asp2(a) and Hu-Asp2(b) polypeptides have the complete amino acid sequence of SEQ ID No. 2, SEQ ID No. 4, and SEQ ID No. 6, respectively; and

(b) a nucleotide sequence complementary to the nucleotide sequence of (a).

The nucleic acid molecule of claim 92, wherein said Hu-Asp polypeptide is Hu-Asp1, and said polynucleotide molecule of 1(a) comprises the nucleotide sequence of SEQ ID No. 1. The nucleic acid molecule of claim 92, wherein said Hu-Asp polypeptide is Hu-

Asp2(a), and said polynucleotide molecule of 1(a) comprises the nucleotide sequence of SEQ ID No. 4. The nucleic acid molecule of claim 92, wherein said Hu-Asp polypeptide is Hu-Asp2(b), and said polynucleotide molecule of 1(a) comprises the nucleotide sequence of SEQ ID No. 5. An isolated nucleic acid molecule comprising polynucleotide which hybridizes under stringent conditions to a polynucleotide having the nucleotide sequence in (a) or (b) of claim 92. A vector comprising the nucleic acid molecule of claim 96. The vector of claim 97, wherein said nucleic acid molecule is operably linked to a promoter for the expression of a Hu-Asp polypeptide. The vector of claim 98, wherein said Hu-Asp polypeptide is Hu-Asp1. The vector of claim 98, wherein said Hu-Asp polypeptide is Hu-Asp2(a). The vector of claim 98, wherein said Hu-Asp polypeptide is Hu-Asp2(b). A host cell comprising the vector of claim 98. A method of obtaining a Hu-Asp polypeptide comprising culturing the host cell of claim 102 and isolating said Hu-Asp polypeptide. An isolated Hu-Asp1 polypeptide comprising an amino acid sequence at least 95% identical to a sequence comprising the amino acid sequence of SEQ ID No. 2. An isolated Hu-Asp2(a) polypeptide comprising an amino acid sequence at least 95% identical to a sequence comprising the amino acid sequence of SEQ ID No. 4. An isolated Hu-Asp2(a) polypeptide comprising an amino acid sequence at least 95% identical to a sequence comprising the amino acid sequence of SEQ ID No. 8. An isolated antibody that binds specifically to the Hu-Asp polypeptide of any of claims 104-107.

Here we disclose numerous methods to assay the enzyme.

A method to identify a cell that can be used to screen for inhibitors of  $\beta$  secretase activity comprising:

(a) identifying a cell that expresses a protease capable of cleaving APP at the  $\beta$  secretase site, comprising:

- i) collect the cells or the supernatant from the cells to be identified
- ii) measure the production of a critical peptide, where the critical peptide is selected from the group consisting of either the APP C-terminal peptide or soluble APP,
- iii) select the cells which produce the critical peptide.

The method of claim 108 where the cells are collected and the critical peptide is the APP C-terminal peptide created as a result of the  $\beta$  secretase cleavage. The method of claim 108 where the supernatant is collected and the critical peptide is soluble APP where the soluble APP has a C-terminal created by  $\beta$  secretase cleavage. The method of claim 108